Practical Management of the Stone-Former

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• *The recurrence or growth of urinary calculi may be prevented by a plan of management suited to the stone-forming tendency of the patient.*

SINCE SURGICAL REMOVAL of urinary calculi is directed against the effect of the disease and usually leaves the cause unaltered, recurrence may be anticipated in from 25 to 40 per cent of all cases.[8] It is imperative, therefore, to use what measures are possible to alter the obscure processes that lead to formation of calculi.

Since any plan of intelligent management is based on the composition of the calculus, the first essential is to know the particular kind of stone formed in each case. Usually if there is recurrence the kind of calculus formed is the same as the first, and if conditions can be changed to alter the urinary milieu which initially led to formation of a calculus, many recurrences will be prevented.

As it provides the most accurate data regarding the composition of calculi, chemical analysis should be carried out on all stones removed or passed. It is important to impress patients with the necessity of recovering calculi that are passed spontaneously. Simple qualitative chemical analysis usually provides all the information needed. More complicated quantitative analyses give little additional information of value as concerns treatment. When calculi cannot be obtained, something concerning their nature may be predicted by the radiographic appearance or by such contributory evidence as the pH of the urine or the type of any complicating infection.

For the purposes of clinical diagnosis and management it is convenient to divide calculi into two large groups, those that are relatively radiopaque, and those that are relatively nonopaque. There are two main types of radiopaque calculi: (1) primary calcium calculi—those usually combined with oxalates, phosphates or carbonates; and (2) secondary magnesium ammonium phosphate stones which form in the presence of strongly alkaline urine. Three types of calculi are relatively nonopaque: the more common uric acid stones and cystine stones, and the extremely rare xanthine stones.

The initial step in the study of any patient with calculus is to determine whether he has any metabolic disease or predisposing factor which might lead to stone formation. Since the diagnosis of metabolic disease is often difficult, there is a tendency to subject patients to innumerable, time-consuming, expensive laboratory tests, many of which have no practical application. In the authors' plan of observation only the few laboratory procedures that are essential are used.

As concerns radiopaque calculi, there is usually little difficulty in differentiating primary calcium calculi from the magnesium ammonium phosphate group. The former are usually discrete calculi which form in neutral or slightly alkaline urine in the absence of infection. The latter form in strongly alkaline urine and are frequently caused by stasis and alkaline infection with urea-splitting organisms or by high alkali ingestion. The phosphate calculi may be branched and of stag-horn conformation, similar in appearance to some cystine calculi, which also may be slightly radiopaque.

The most important chemical test in the study of patients with primary calcium calculi is the quantitative determination of urinary calcium. This is the one test which gives indication of one or more of the causes of hypercalcuria: (1) Hyperparathyroidism; (2) excessive calcium intake; (3) excessive vitamin D intake; (4) immobilization; (5) renal tubular acidosis, from pyelonephritis, nephrocalcinosis, or congenital tubular defect; (6) sarcoidosis; (7) idiopathic.

As a pilot test, quantitative calcium, phosphorus and creatinine determinations are made of urine collected over a 24-hour period, without varying the patient's usual diet or fluid intake. Although these determinations are of no diagnostic significance as concerns metabolic disorder, when repeated to allow for variations in the patient's diet, they provide useful background information. In the first phase, information is gained of the normal 24-hour creatinine output for the particular individual. Regardless of food ingested, the 24-hour creatinine output does not vary more than 200 mg. (normal 1 to 2 gm). This serves as a check that the entire 24-hour urinary output is obtained at subsequent

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TABLE 1.—*Menu for low calcium test diet (to be taken for 4 consecutive days)*

Composition of Meal Pattern: Calcium 175 mg., Phosphorus 894 mg., Calories 2400.

Breakfast:	
Orange juice*	½ cup (scant)
Cooked Farina	½ cup
with sugar	2 teaspoons
Soda crackers	3 squares
Butter	3 pats (6 teaspoons)
Bacon	3 slices
Sugar	3 teaspoons
Coffee	
Dinner:	
Plainly cooked beef†	2½ ounces
Boiled or baked potato	¼ cup
Raw or canned tomato	1 small or ½ cup canned
Soda crackers	3 squares
Butter	3 pats (6 teaspoons)
Applesauce with sugar*	½ cup
Sugar	3 teaspoons
Tea	
Supper:	
Plainly cooked lamb†	2½ ounces
Rice	1 scant cup
Corn	1 large ear or ½ cup frozen
Soda crackers	3 squares
Butter	3 pats (6 teaspoons)
Banana*	1 small
Sugar	3 teaspoons
Tea	

This diet is to be taken for three consecutive days prior to collecting a 24-hour specimen of urine and the day of collecting the urine. The first thing on the morning following three days of diet, void and discard urine. Thereafter collect *all* of urine passed during the next 24 hours. Collect in clean 1 gallon glass jug. This includes *all* urine passed up to and including first urine passed the morning after the day of starting the collection.

*Bananas, oranges, peaches, applesauce or watermelon may be used.
†Beef, lamb, veal, or chicken may be used.

determinations. Secondly, this initial study gives indication of the amount of calcium and phosphorus a patient excretes on his usual diet.

In hyperparathyroidism, calcium excretion exceeds intake, even on a low-calcium diet. To diagnose or rule out this condition, the patient is given a diet of 175 mg. of calcium daily (Table 1) for four days; the urine is collected during the last 24-hour period and a quantitative calcium determination made.[4] (We are attempting to develop a simple office test for this determination. In our experience the Sulkowitch test is not sufficiently sensitive for quantitative estimates.) If the 24-hour specimen, with the patient on the test diet, contains more than 200 mg. of calcium, the diagnosis of hyperparathyroidism is likely. The serum calcium and phosphorus should also be measured to give additional confirmatory evidence. If the amount of calcium in the urine is only slightly excessive the concentration in the serum may be normal. However, in advanced cases of hyperparathyroidism, the serum changes will be quite evident.

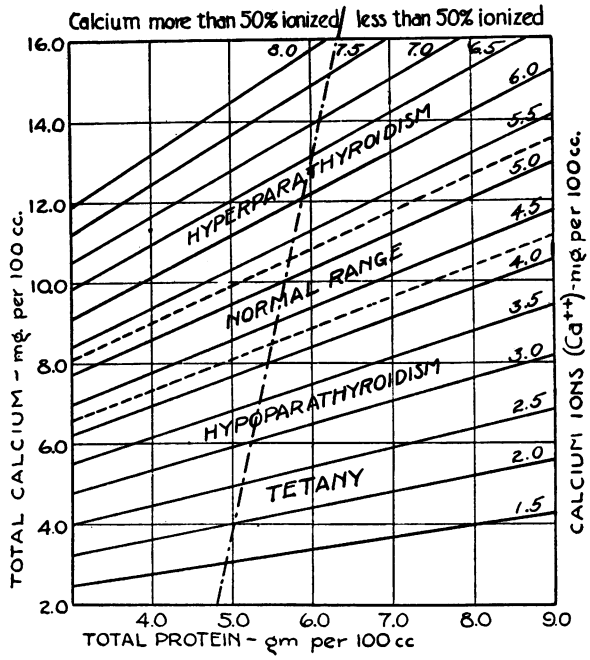

Chart 1.—Urinary calcium excretion after 175 mg. diet for three days. Preoperatively, 570 mg. were excreted in 24 hours. After operation there was a normal excretion of 154 mg. in 24 hours.

The normal value for serum calcium is 9 mg. to 11 mg. per 100 ml. and for serum phosphorus 3 mg. to 5 mg. per 100 ml. In hyperparathyroidism, while serum calcium is increased and serum inorganic phosphorus decreased, the urinary output of both calcium and phosphorus is increased. The mode of action is not entirely clear, but it has been found in animals that injection of parathyroid hormone causes hyperphosphaturia, probably by decreasing the renal threshold for phosphate excretion.[1] Apparently the sequence of events is as follows: First hyperphosphaturia occurs, producing hypophosphatemia; then, since there is a constant ratio between serum phosphorus and calcium, a decreased serum phosphorus causes hypercalcemia, which in turn leads to hypercalcuria. An additional factor is an increased amount of calcium in the serum and urine caused by increased osteoclastic activity under excess parathyroid hormonal stimulus.

Since the serum calcium determination represents total serum calcium and since the diagnosis of hyperparathyroidism depends solely on the amount of ionized calcium, whenever the diagnosis is doubtful the amount of ionized calcium is computed by determining the amount of serum protein, to which nonionized protein is bound. A low-serum protein (normal is 6 to 8 gm. per 100 ml.) indicates that a borderline total serum calcium contains a more significant amount of ionized calcium. When the total serum calcium and the serum protein are calculated,

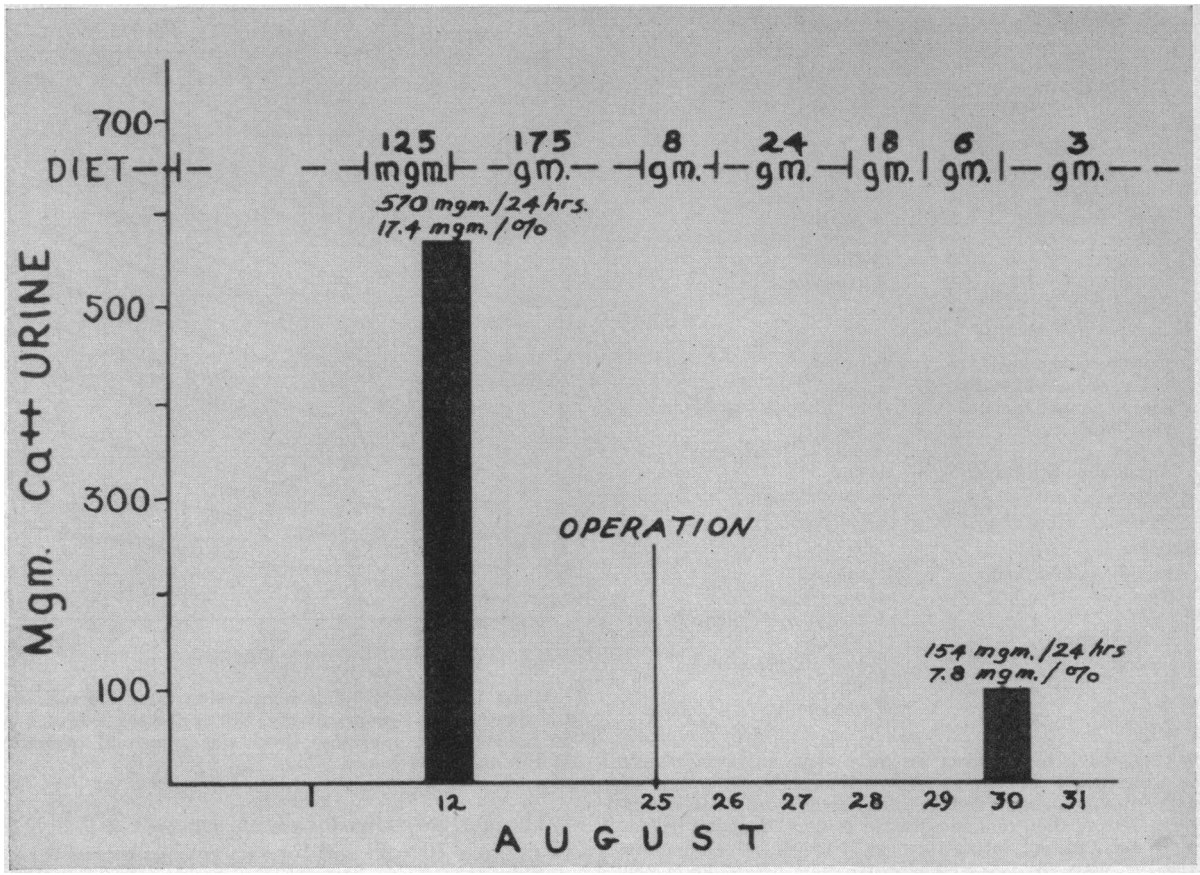

Chart 2.—Serum studies showing initially elevated calcium and decreased phosphorus with prompt return to normal after partial parathyroidectomy, when supplementary calcium feedings were discontinued.

the ionized fraction may be computed from a chart (Chart 1).[6]

The serum alkaline phosphatase is not diagnostic of parathyroid disease and indicates only the amount of osteoblastic activity. Likewise, the urinary phosphate excretion is useless in the diagnosis of hyperparathyroidism, although it serves as an important guide in the prevention of calculi.[7] Most renal changes in metabolic disease are secondary to hypercalcuria, and the urinary phosphate excretion is not consistently abnormal. Moreover, in the idiopathic stone-former, the amount of phosphate excreted depends almost entirely on the amount ingested.

Although hyperparathyroidism is the cause in fewer than 5 per cent of cases of calcium calculi, it is extremely important to determine whether or not this condition is present, for, if it is, permanent cure is attained by partial parathyroidectomy.

Hyperparathyroidism is so insidious that it frequently escapes detection even though the patient may be under medical observation, as for urolithiasis. A typical case is that of a 59-year-old housewife who after passing innumerable calculi over a period of four years, was finally admitted to the hospital for study. At the time of entry, x-ray studies revealed

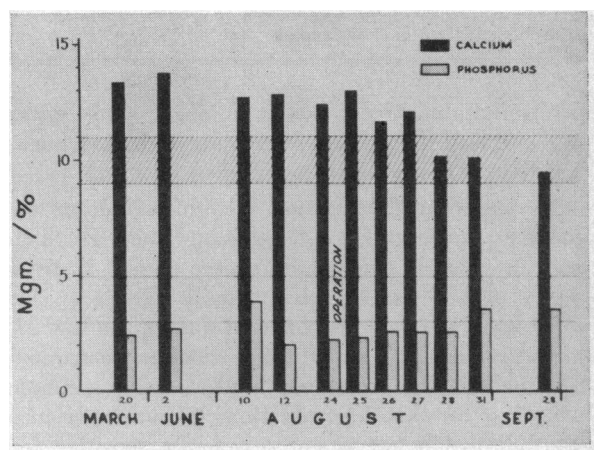

Chart 3.—For calculation of ionized fraction of calcium when total serum calcium and protein are known (McLean and Hastings).

calculi in both kidneys. On the four-day regulated calcium diet, the patient's urinary calcium excretion was abnormally high (Chart 2). Studies of the serum revealed hypercalcemia and hypophosphatemia (Chart 3). The diagnosis was hyperparathyroidism.

Even though no calculi are recovered for chemical analysis, the careful study of the individual patient,

including the history, physical examination, urine examination, x-rays and cystoscopic studies, supplemented by the special chemical tests made to rule out hyperparathyroidism, is usually adequate to differentiate between calcium and magnesium ammonium phosphate calculi and also to pin-point any evident etiologic factor which might cause hypercalcuria.

Excessive calcium intake may occur with the ingestion of large quantities of milk, cream and alkalis, as in the treatment of peptic ulcer. Excessive vitamin D intake causes large quantities of calcium to be absorbed from the large intestine, with increased phosphorus and calcium excretion in the urine. This also occurs in acidosis. Forced immobilization of the skeleton, as when patients are in a cast or in traction, produces bone resorption with excretion of large quantities of calcium. Renal tubular acidosis, seen in pyelonephritis, nephrocalcinosis or a congenital tubular defect causes an inability of the tubules to produce ammonia, excrete hydrogen ion, or concentrate the urine. There is loss of fixed base in the form of increased calcium and potassium excretion. Hypercalcuria in sarcoidosis is apparently caused by invasion of osteoblasts and demineralization. In idiopathic hypercalcinuria there is apparently a reduced renal threshold to calcium excretion since the serum levels are normal and acidosis is not present.

There is no apparent metabolic cause for magnesium ammonium phosphate calculi—the usual etiologic factors being stasis and alkaline infection.

As concerns study of patients with relatively nonradiopaque calculi, the same general rules of study apply. The first step is to determine the presence of any underlying metabolic disease or etiologic factor.

Uric acid calculi which form in the kidney and ureter are usually caused by a metabolic error in purine metabolism. This is in contrast with uric acid calculi of the urinary bladder which result from stasis. The urine is acid and usually uninfected. In many cases there is an increased level of uric acid in the blood without increased urinary excretion, as sometimes occurs in gout. In some instances, however, there is an elevation of the serum uric acid (normal 2 to 4 mg. per 100 ml.) and increased urinary excretion, normally 0.3 to 1.2 gm. for 24 hours.

Cystine calculi result from an intermediary protein metabolic defect in which incomplete oxidization of cystine is followed by the increased urinary excretion of crystalloids and formation of stones. About 2.5 per cent of patients with cystinuria have calculi.[5] These stones are frequently stag-horn and slightly radiopaque. The urine is acid and usually uninfected. The diagnosis may be made by an elevated 24-hour urinary output of cystine[3] (normal 10 to 15 mg.).

Although it may not be advisable to place every patient who forms a calculus on an intensive prophylactic regimen, the authors consider the following indications mandatory:

1. One or more recurrences.
2. One kidney removed because of calculous disease.
3. Calculi in a single kidney (other kidney absent or removed for whatever cause).
4. Calculi present but operation refused or not considered practical.
5. Presence of residual urinary infection or obstruction which is impossible to eliminate following removal of calculus.

For the success of any plan of prevention, two objectives must be attained: The prevention of a nidus for a calculus to form, and the prevention of crystalloid concentration sufficient for precipitation on a nidus.

Some measures are effective regardless of the type of calculus:

1. The ingestion of large quantities of fluids. Patients should be advised to take three to four quarts of fluid daily, with instructions to distribute the intake over the waking hours as evenly as possible—one glass or more every hour. This maintains a constantly low concentration of urine. The more dilute the urine, the less the likelihood of crystalloid precipitation. This measure is also helpful in combating urinary infection.
2. The desirability of eliminating any complicating infection, obstruction or stasis is obvious.
3. Physical activity is essential. Since recumbency causes loss of calcium and phosphate in the urine, it is a factor in promoting the growth of all types of calculi. In patients with spinal cord or orthopedic difficulty, provisions should be made for ambulation or similar physical activity.

When ambulation is not practical, administration of hyaluronidase may possibly prevent calculus formation during the initial period of recumbency when calcium metabolism in the bones is being restabilized and excess calcium in the urine is inevitable.[2] When this enzyme is injected subcutaneously, hyaluronate is released from the site of injection and subsequently reaches the urine. Dosage may be regulated according to the amount necessary to clear the urine of turbidity and sediment. It varies between 150 and 900 turbidity-reducing units every 24 to 48 hours. This substance, acting as a protective colloid, is said to disperse the crystalline matter already present in the urine and to inhibit the formation and growth of new crystalline matter. (The authors have not found hyaluronidase useful in other circumstances, and are not certain of its use in recumbency.)

The following measures apply to patients with a tendency to form radiopaque calculi:

1. Patients with calculi composed of phosphorus or calcium are placed on the low-phosphorus diet advocated by Shorr.[7] Since foods low in phosphorus are usually low in calcium as well, the excretion of urinary calcium as well as phosphorus is reduced. A particular advantage of a low-phosphorus diet is its safety in cases of renal impairment in which an acid-ash diet would be dangerous. In patients with de-

TABLE 2.—*Low phosphorus menu pattern*

(Approximately 2000 calories, with 75 grams protein)

GENERAL RULES

1. Drink large quantities of fluids: 3 to 4 quarts per day.
2. Limit intake of food of highest phosphorus content: meat, fish, fowl, eggs, milk and cheese. The suggested menu pattern supplies approximately 2000 calories, 75 grams protein, 900 milligrams phosphorus and 345 milligrams calcium.
3. Take 2½ tablespoons (1½ ounces or 45 ml.) Basaljel 4 times daily; one hour after meals and at bedtime.
4. Take one capsule daily of one of the following vitamin preparations: Unicap, Upjohn; Vita Kaps Improved, Abbott; Stanford Vitamin Capsule.

FOODS PERMITTED	FOODS EXCLUDED
Beverages: Artificial fruit ades, carbonated beverages, coffee, lemonade, tea. 3 to 4 quarts daily. Whiskey if desired.	Ale, beer, brandy, milk drinks, postum.
Bread: White bread, white rolls, raised doughnuts. Five slices of bread daily.	Hot breads, biscuits, muffins, pancakes, waffles, whole grain breads.
Cereal: Refined cereals as cornflakes, cornmeal, regular cream of wheat, Farina, rice krispies; use 1 serving as substitute for 1 slice bread.	Whole grain cereals, bran, oats, wheat.
Condiments: As desired.	
Dairy Products and Eggs: Use ½ cup milk, or 1 egg, or ¼ cup cottage cheese, or 3½ ounces cream cheese or 2 ounces Camembert.	Processed cheddar, cheese food, processed Swiss.
Desserts: Apple betty, angel cake, apple or blueberry pie, sherbet, ices.	Cake, ice cream, cream pies, pudding.
Fats: Butter, hydrogenated fat, brown gravy, lard, margarine, French dressing, hard sauce.	Gravies, dressing or sauces made with milk or eggs; nuts.
Fruits or Fruit Juices: 1 serving citrus; 1 to 2 servings apple, apricot, berries, cherries, grapes, melon, peach, pear, pineapple, plums or tangerines.	Currants, prune juice, raisins.
Meat, Fish or Fowl: 6 ounces. Beef, chicken, lamb, pork, sausage or fish or shellfish such as: bass, clams, cod, crab, flounder, haddock, herring, lobster, oyster, scallop.	Broilers, dried beef, liver, sardines, sweetbreads.
Potato or Substitute: ½ cup serving as desired.	Creamed or scalloped.
Soup: 1 serving. Bouillon, chicken-noodle, chicken-rice.	Bean, beef or vegetable. Cream soups.
Vegetables: 3 servings. Beets, cabbage, carrots, cucumber, green beans, green leafy vegetables, pepper, rutabagas, scallions, squash, tomatoes, turnips.	Artichoke, lentils, mushrooms, peas, soybeans.

Note: Foods not listed should be used only occasionally and in limited quantities; avoid phosphate laxatives, phosphate baking powders, self-rising flours.

SUGGESTED MENU PATTERN

Breakfast:	Mg. Phosphorus
Orange juice, 6 oz.	30
Cereal, fine, 1 serving	22
Toast, white, 1 slice	21
Butter, 1 teaspoon	1
Jelly, 1 tablespoon	2
Milk and cream (half and half)	104
	180
Lunch:	
Sandwich:	
Meat, 2 oz.	130
Bread, white, 2 slices	42
Butter and mayonnaise	4
Vegetable or salad	35
Fruit	25
Sugar, coffee, tea	0
	236

Alternate Breakfast:	Mg. Phosphorus
Orange juice, 6 oz.	30
Egg, 1	105
Toast, white, 2 slices	42
Butter, 1 tablespoon	2
Jelly, 1 tablespoon	2
Sugar, coffee, tea	0
	181
Dinner:	
Soup or fruit cocktail	25
Meat, fish or fowl, 4 oz.	260
Potato or paste, ½ cup	56
Vegetable, ½ cup	35
Salad	35
Hard roll, 1	25
Butter, seasonings	4
Dessert	35
Sugar, coffee, tea	0
	475

Approximate total 892 milligrams phosphorus.

Between Meals: Plain gelatin, lemonade, artificial fruit ades, water to bring fluid intake to 3 to 4 quarts per day.

creased renal function, acidosis tends to develop because of the retention of acid radicals (phosphate, sulfate, organic acids, urea). An acid-ash diet would aggravate the acidosis and throw the extra burden of excreting excess acid on already damaged kidneys. In order to make the diet as palatable as possible, the authors have attempted to incorporate a wide selection of foods. The diet contains approximately 2,000 calories, with 75 gm. of protein and less than 1 gm. of phosphorus (Table 2). To patients who wish to calculate their own diets, we give a more complicated diet form which lists the phosphorus content of all foods.*

While the patient is on this diet, the 24-hour urinary output should ideally contain less than 300 mg. of phosphorus. Determination of the phosphorus excretion is the guiding test in the control of the Shorr regimen. This is made every few weeks until the excretion becomes stabilized.

As a check that all the 24-hour urine has been collected, creatinine excretion is also measured. It should fall in the range which is constant for each patient. There is no evidence that a constant dietary reduction of phosphate gives rise to hypophosphatemia or its sequelae, but the authors are investigating this question further.

2. As an adjunct to the low-phosphorus diet, Shorr management consists of administering an aluminum gel — aluminum carbonate being the most effective—to divert phosphorus from the urine to the bowel. Aluminum carbonate (Basaljel®) acts with phosphate by absorption to form insoluble aluminum phosphate. The more Basaljel the patient takes, the more latitude may be permitted in the matter of diet. Thirty to 40 ml. of Basaljel four times daily, one hour after meals and at bedtime, is the average dose. To make it more palatable, the patient is instructed to flavor it with lemon juice or a Kool-Aid powder. For a few weeks constipation occurs but it gradually abates. Fruit juices or a mild cathartic such as cascara may be given in the early stages of this treatment.

The authors have not found any tablets as effective as Basaljel liquid, but if patients will not cooperate in taking the liquid, Aludrox® may be substituted. One tablet is slightly less effective than one teaspoon of Basaljel.

3. Because of the theoretical possibility that vitamins may help to preserve a normal urothelium and prevent nidus formation, such as Randall's subepithelial calcium plaque, patients are given a multivitamin preparation, one capsule daily.

*Authors will supply copies of this diet on request.

4. In the absence of infection, acidification of the urine is not necessary with this regimen. However, if the urinary phosphate cannot be adequately decreased, or if urea-splitting organisms are present and magnesium ammonium phosphatic calculi are forming, acidification of the urine with some form of mandelic acid or ammonium chloride or an acid-ash diet is indicated. Aluminum carbonate tends to alkalinize the urine.

The specific measures for the management of patients with the relatively nonradiopaque cystine, uric acid and xanthine calculi are much the same for all three types of stones.

1. Since these calculi form in acid urine, measures are taken to alkalinize the urine, maintaining the pH at from 7 to 7.5. This is accomplished by either or both of two measures: Either the administration of 4 to 12 gm. of sodium citrate or sodium bicarbonate daily, or by an alkaline-ash diet.

Testing the urine with nitrazine paper is a convenient method for the patient to determine the efficacy of these measures.

2. A low-purine diet aids in reducing cystine, uric acid and xanthine output even though the primary defect is metabolic, not purine intake. In fact, uric acid is excreted by persons on a purine-free diet. In gout, drugs such as acetylsalicylic acid in a dose of 4 to 6 gm. daily or colchicine in acute attacks of arthritis also tend to lower the blood uric acid level and probably the urinary excretion. Smaller doses of acetylsalicylic acid may cause uric acid retention in the blood.

As with radiopaque calculi, the ingestion of large quantities of fluids is essential.

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